Managing the Spectrum of Surgical Pain: Acute Management of the Chronic Pain Patient

William A Olorunto, MD, RPH, Susan Galandiuk, MD, FACS

Postsurgical pain is an unintended side effect of operations that continues to be undertreated, despite new advances in pain management.[1] In treating surgical patients who are on medications for chronic pain, it is important to realize that most of these patients have developed a significant degree of tolerance, thereby requiring much higher doses of opiates than opiate-naive patients. In the United States, it is claimed that chronic pain affects over 70,000,000 patients, and acute pain can lead to chronic pain if not treated properly.[2,3] Pain management in patients on medications for chronic pain requires a multimodal approach, with frequent assessments to ensure adequate pain control.

The objective of this article is to discuss management of acute pain, with an emphasis on patients who are on medications for chronic pain before an operation.

PREOPERATIVE EVALUATION

In evaluating the chronic pain patient preoperatively, it is important to differentiate between tolerance, which is a pharmacologic effect with which increasing doses of analgesic are required to maintain the same level of analgesia and physical dependence, in which withdrawal symptoms will develop if medication is abruptly stopped or an antagonist given.

Preoperative warnings of potential pain management problems include the patient who is on an anxiolytic therapy and patients with any type of chronic pain. This is especially true of back pain patients who have undergone multiple back operations; abdominal pain patients, particularly those with long-standing Crohn's disease or recurrent cancer; and patients with chronic joint pain, such as those with severe rheumatoid or degenerative arthritis. If heavy opioid use is suspected, one should also consider an "all schedule prescription electronic reporting" system, which, for example, is called "KASPER" in Kentucky. This is a Web-based system that tracks all controlled substances dispensed by any licensed pharmacist in Kentucky. It was designed to stop those patients who abuse prescription drugs by soliciting such medications from different physicians in the state. The eKASPER system is available to health-care professionals at all hours of the day and allows physicians and pharmacists to intervene whenever they suspect a pattern of drug abuse by patients. Many other states have similar systems.[4] Physicians can obtain a complete electronic record of all scheduled narcotics that have been filled by a patient within that state. When chronic pain and opioid-consuming patients undergoing urologic, gynecologic, orthopaedic, or general surgery procedures were compared with control patients who were not taking such medications, patients on patient-controlled analgesia (PCA) required a dose over threefold higher than those who were not taking pain medication chronically.[5] Knowing that such a problem may exist makes perioperative pain management safer and more effective.

DIFFERENT TYPES OF PAIN

There are obviously different types of pain. Nociceptive pain is pain that is caused by an injury that stimulates pain receptors and may also be accompanied by inflammation. Nociceptive pain arises when nociceptors are stimulated by noxious stimuli. Nociceptors are present in all tissues and organs except the nervous system. Nociceptive pain can be visceral (eg, pain caused by small bowel obstruction or surgical injury) or it can be somatic (eg, associated with aching bones, joints, and muscle). Neuropathic pain is secondary to an abnormal sensory process that may affect peripheral or central nerves. One example of neuropathic pain often seen in cancer patients is pelvic or leg pain related to direct compression of nerves by cancer or direct invasion. One can also have mixed somatic and neuropathic pain, such as that which can occur after an operation.

PAIN MANAGEMENT

Advantages of effective pain management include increased patient comfort and satisfaction.[6–8] Because of

Competing Interests Declared: None.

Received April 29, 2005; Revised August 1, 2005; Accepted August 8, 2005.
From the Department of Surgery, University of Louisville School of Medicine, Louisville, KY.
Correspondence address: Susan Galandiuk, MD, Department of Surgery, University of Louisville School of Medicine, Louisville, KY 40292.

ISSN 1072-7515/06/$32.00
doi:10.1016/j.jamcollsurg.2005.08.007

this increased patient comfort, effective pain management is also associated with earlier patient mobilization,[9] decreased hospital stay,[8,9] and decreased cost.[9] Gastrointestinal and urinary effects of acute pain are primarily a result of sympathetic overactivity. This, in turn, leads to increased urinary sphincter activity, which then can result in urinary retention. Sympathetic overactivity can also result in increased intestinal secretions and increased smooth muscle sphincter tone within the gastrointestinal tract, which then decreases intestinal motility.[10,11]

Pain management in the elderly

In assessing acute pain in chronic pain patients, one must always account for the effect of age. Increased age, which all physicians continue to see more frequently as our population ages, increases both the surgical risk and the side effects of narcotics. There is a decreased cardiac and pulmonary reserve with increasing age and an increase in the incidence of confusion when these patients are given opioids postoperatively, all serious potential complications. Because most elderly patients are on multiple medications, prescribing in this population can be challenging. Incidence of adverse reactions is higher in the elderly and increases as the number of medications increases. An elderly patient taking six medications is likely to have adverse reactions 14 times more than a younger person taking the same number of medications.[12]

The additive respiratory depressant effect of both opiates and anxiolytics must be taken into consideration. In addition, most elderly patients metabolize drugs at a slower rate, requiring less-frequent dosing and a reduction in dosage to avoid pronounced adverse effects. There are also certain medications that should be avoided in elderly patients, based on their adverse effects profile. Meperidine is associated with more sedative effects in the elderly and with an increased risk of falls compared with other opiates.[13] It should be avoided in the elderly patients. Constipation is one of the side effects of opiates and nonsteroidal antiinflammatory drugs. Elderly patients with already reduced gastrointestinal motility can have a worsening of constipation with pain medications. It is imperative that once patients are able to tolerate oral pain medications, stool softener or bulk laxatives be a part of their pain regimen. The important concept with pain management in the elderly is to start at a lower dose (generally 50% of the usual dose), and increase the dose to maximize pain relief while minimizing adverse effects.

TIME AND MODE OF ADMINISTRATION OF ANALGESIA

Perioperative pain control can occur at three specific intervals with respect to surgery: pre-, intra-, and postoperatively. Most surgeons are fairly adept at addressing pain-treatment needs of a patient postoperatively, but the first two opportunities continue to be largely ignored.

There are many different routes of administration of analgesia to improve perioperative pain control. These different routes of drug administration include epidural administration, continuous IV administration with or without patient-controlled pumps, transdermal analgesic administration, sublingual analgesic administration, and incisional analgesic administration. Addition of other agents or devices includes administration of preoperative sedatives; administration of nonsteroidal antiinflammatory drugs, either intraincisionally, orally, or IV; and use of devices such as transcutaneous electric nerve stimulation. In one study that examined the effect of preoperative sedatives, 55 patients were randomized to receive either 5 mg midazolam or placebo at least 30 minutes preoperatively. Patients who were pretreated had a greater decrease in postoperative pain and greater decrease in postoperative anxiety.[14]

Incisional pain treatment

Incisional therapy is underused and can be very effective. This should occur during the operation with the direct judicious injection of local anesthetics, opiates, or nonsteroidal antiinflammatory drugs into the incision or fascia, or it can occur postoperatively through continuous subcutaneous infusion of local anesthetic or with use of local anesthetic patches. When 30 patients undergoing outpatient inguinal hernia repair were randomized to receive 60 mg ketorolac, either IV or into their surgical site, patients who received this medication into their surgical site had increased time for requesting their first analgesic and decreased oral analgesic consumption.[15] In a study that compared lidocaine to tramadol subcutanous injection, tramadol was shown to be as effective as lidocaine in reducing the amount of postoperative analgesia used by patients.[16] Lidocaine (1 mg/kg), ketorolac (60 mg), tramadol (2 mg/kg), and morphine (2 to 4 mg) are commonly used subcutaneously for preincisional analgesia.

Continuous local anesthetic delivery through intraincisional infusion catheter is now widely available. In a retrospective study involving 49 patients having mastec-

tomies over a 5-year period, analysis of the need for postoperative analgesia was performed. As much as 68% of patients with the intraincisional infusion catheter did not require postoperative analgesic on postoperative day 1 compared with 11% in the control group (n = 27) without local anesthetic infusion. Total dose of equivalent opiate used was also much less in the group with incisional infusion catheter compared with the control group.[17] This local anesthetic infusion system is available for use in many types of specialty operations. Note that the report includes only 49 patients selected over a 5-year period.

Epidural analgesia

Epidural analgesia is very effective in pain management of patients who have undergone major abdominal, thoracic, orthopaedic, or obstetrics and gynecologic operations. Postoperative epidural analgesia provides better pain management, with a lesser degree of sedation, less postoperative ileus after abdominal operation, and improved pulmonary functions compared with IV opiates.[18] In a study that randomized 64 patients undergoing elective colonic resection to receive either PCA pump or epidural analgesia, patients in the epidural group had lower postoperative pain as assessed by visual analogue scale; better mobilization out of bed; and earlier return of bowel function.[18] Epidural analgesia is not without contraindications and complications. Some of the serious complications of epidural anesthesia include epidural abscess and epidural hematoma.[19] In the advent of the morphine sulfate extended-release liposome injection (depoDur), the epidural route of analgesic administration could potentially become quite attractive to patients. This liposomal morphine sulfate formulation is designed for a single-dose epidural injection and is intended for management of postoperative pain after major operations. A single-dose injection into the epidural space can provide pain relief for up to 48 hours.[20] The advantage of this single-dose injection is enormous compared with traditional continuous epidural anesthesia. This formulation negates the need for an indwelling catheter, which may serve as a source of infection or may accidentally fall out. Unlike traditional epidural analgesic, which is contraindicated in patients on anticoagulation, morphine sulfate extended-release liposome injection can be injected preoperatively into the epidural space before initiation of anticoagulation therapy. This formulation of epidural morphine is ideal for an orthopaedic patient in need of anticoagulation in the immediate postoperative period.

Parenteral pain medications

Opiates are the most frequently used parenteral pain medications. Parenteral analgesia can be IV, IM, or subcutaneous. In choosing an appropriate opiate drug, one must take into consideration both the intensity and duration of pain therapy desired. Commonly used IV opiates include morphine, meperidine (Demerol), hydromorphone (Dilaudid), and fentanyl. Morphine is considered the prototype for all opioids. It has a rapid onset of action when administered IV. Morphine, unlike other opiates, causes significant histamine release, which leads to its common side effects, including pruritis, nausea and vomiting, and hypotension. It is also used as an adjunct in treatment of pulmonary edema. Meperidine is only about one-tenth as potent as morphine, but with a quicker onset of action, and more respiratory depressant effects. It is metabolized to normeperidine, which is less potent but with a longer half-life. Normeperidine, because of its longer half-life, can accumulate in the blood stream after prolonged use and cause central nervous system excitation, which may lead to seizures. Meperidine, in the acute management of the chronic pain patient, should only be used for a period of 3 days consecutively. One should avoid using meperidine in elderly patients and in patients with renal failure. Of note is that meperidine could induce a life-threatening drug interaction when used in patients who have taken monoamine oxidase inhibitors within 14 to 21 days of meperidine therapy. Fentanyl is a synthetic opioid that is about 100 times more potent than morphine.[21] It has a much faster onset and a very short duration of action. It is ideal for immediate pain relief, dressing changes, and short bedside procedures. Hydromorphone is about eight times more potent than morphine, and with a better side effect profile. It is one of two opiates (oxymorphone is the other one) available for use as rectal suppositories. Tramadol (Ultram) is a centrally acting synthetic analgesic that is available as parenteral and oral formulations. This drug is unique because, even though it is centrally acting, it has only minimal sedative and respiratory depressant effects, unlike opiates.[22] Ketorolac is the only parenteral nonsteroidal antiinflammatory drug available in the United States. It is an excellent medication for moderate to severe pain, either alone or in combination with opiates. Its side effects include gastrointestinal

bleeding and nephrotoxicity. It is contraindicated in patients with a history of renal insufficiency and those with one kidney. Adequate hydration is essential to protect the kidneys, especially in elderly patients.

NSAIDS, cyclo-oxgenase 2 inhibitors

Arachidonic acid is broken down by cyclo-oxgenase (COX) 1 and 2. COX-1 metabolizes arachidonic acid into prostaglandins and thromboxane, which have a protective effect on the gastrointestinal tract and provide for normal platelet function, respectively. Disruption of COX-1 leads to decreased prostaglandin production in the gastrointestinal tract with increased gastrointestinal toxicity as well as decreased thromboxane levels, which results in impaired platelet function.[23] Selective pharmacologic COX-2 inhibition, on the other hand, results in decreased inflammation, pain, and fever without increased gastrointestinal toxicity and impaired platelet function. NSAIDs that are most frequently used for postoperative pain management currently include IV or oral ketorolac and oral ibuprofen. Both of these inhibit both COX-1 and COX-2 and can be associated with GI toxicity and platelet dysfunction. Celecoxib and valdecoxib are oral COX-2 inhibiting nonsteroidal inflammatory agents; valdecoxib being a second-generation COX-2 inhibitor. There are two IV forms of COX-2 inhibitors, including valdecoxib and parecoxib, which have not yet received Food and Drug Administration approvals. Specific COX-2 inhibitors provide for analgesia without the typical side effects of conventional NSAIDs. Table 1 shows oral and IV second- and third-generation COX-2 inhibitors currently in use in Europe and the United States.

On September 30, 2004, the drug rofecoxib (Vioxx) was withdrawn from the market because of findings of increased relative risk of stroke and myocardial infarction.[24] This was determined after 18 months of treatment in a randomized, prospective, placebo-controlled clinical trial designed to assess the efficacy of rofecoxib on the recurrence of colorectal polyps in patients with a history of colorectal adenomas.[24] Valdecoxib (Bextra) has a similar side effect profile as rofecoxib. In a clinical trial database involving approximately 8,000 patients treated with valdecoxib for 6 to 52 weeks, there was an increase in cardiovascular thromboembolic events. Similar to rofecoxib, valdecoxib has also been withdrawn from the market.[25] Celecoxib (Celebrex) also has been associated with this adverse effect but to a lesser extent.

Table 1. Second- and Third-generation COX-2 Inhibitors Available in the United States and Europe

COX-2 inhibitors	Dosage
Celecoxib (Celebrex)	100−400 mg daily po
Valdecoxib (Bextra)*	10−40 mg daily po/IV
Parecoxib	40 mg daily IV

*Withdrawn from market.

Thromboembolic events are both dependent on the dose and duration of treatment. There is currently no consensus on the guideline for prescribing selective COX-2 inhibitors. This recent concern about thrombotic cardiac events may greatly restrict use of these agents in the future. Despite this recent controversy, these drugs remain very important in management of acute pain. We believe that side effects of chronic COX-2 inhibitor use will not interfere with their valuable use in the acute setting, such as before and after major operations. The former involves the growing trend of using "preemptive analgesia," where medications such as COX-2 inhibitors are administered preoperatively to block the pain response rather than waiting until the pain occurs and then treating it.

Adjuvant analgesics

The concept of using "adjuvant analgesics" is especially important in caring for the chronic pain patient undergoing an operation. "Adjuvant analgesics" refers to drugs that are developed for a primary indication other than pain, but that produce analgesic effects in specific circumstances. Anticonvulsants can be used in this manner.[26] A useful drug in this category is gabapentin (Neurontin). Gabapentin is renally excreted and has few known drug interactions; it can lead to sedation. Doses up to 3,600 mg gabapentin can be given in a 24-hour period. This agent is particularly helpful in patients who have neuropathic pain, such as patients with recurrent rectal cancer or phantom pain after limb amputation. In this category, one also can use valproic acid (Depakote) and phenytoin (Dilantin), both of which have the advantage that one can monitor plasma concentrations. Antidepressants can also be used as adjuvant analgesics; tricylics being the safest. These drugs can have anticholinergic effects and also can cause somnolence. Amitryptiline is a safe medication in this category and can be used in doses of 10 to 200 mg/day. Other safe drugs in this category include imipramine or doxepin.[27]

Transdermal applications

Transdermal administration of analgesics such as fentanyl through skin patch is very useful in chronic pain patients. The amount of fentanyl that is released transdermally is proportional to patch surface area. Patches are manufactured in 25, 50, 75, and 100 μg per hour release strengths. The 100 μg per hour patch is roughly equivalent to the IV administration of 2 to 4 mg morphine sulfate per hour.[28] Importantly, there is a delay between initial patch placement and the time when clinically relevant plasma levels are achieved. A patient-controlled transdermal analgesia, which is currently under development, consists of a self-contained preprogrammed PCA system.[29] It is a credit-card−sized unit that can be applied to the skin of the upper arm or chest. This system (E-TRANS) uses iontophoresis (ie, electrotransport technology) to deliver fentanyl into tissue by means of an electric current. Iontophoresis can provide relatively rapid systemic drug delivery on demand, which is a major advantage over the traditionally passive transdermal systems. Dosing of analgesia is initiated whenever the patient presses the button on the system twice within 3 seconds. This transdermal PCA system remains active for 24 hours or until 80 doses have been delivered, whichever comes first. Two dosage forms have been developed and are capable of delivering 40 or 25 μg of fentanyl over a 10-minute period with a maximum of 6 doses per hour. Transdermal fentanyl patches are associated with less nausea and less decrease in gastrointestinal motility than with IV opioids. In patients with generalized edema, there is decreased effectiveness with transdermal medication. There is also more rapid absorption in patients who have an increased skin temperature. In one study, fentanyl patches were placed preoperatively in patients undergoing abdominal operation and compared with placebo patches. Postoperatively, both pain on movement and pain at rest were assessed. Significantly less parenteral analgesics were necessary in patients receiving preoperative fentanyl patches.[30] Use of lidocaine patches will most likely increase over time. Currently, the only FDA-approved indication for such patches is postherpetic neuralgia. These 10 × 14-cm felt patches can be cut to a size appropriate to treat the painful area. They contain 700 mg aqueous-based lidocaine, and up to 3 patches can be applied per day for 12 hours at a time. The manufacturer recommends placing them directly on the painful area for 12 hours and then leaving the skin without a patch for the next 12 hours. With this method of administration, low doses of lidocaine diffuse directly into the epidermis and dermis.[31] This is thought to reduce abnormal, spontaneous, and evoked activity of damaged efferents through sodium channel blockade. This acts locally on damaged nerves and soft tissue underlying the patch and produces analgesia without numbness of the skin to which it is applied. There is minimal (2% to 3%) systemic absorption.[32] Absorption is related to duration of application and to the amount of covered surface area. In one study, when these patches were applied to healthy volunteers, a mean peak blood concentration approximately one-tenth that was needed for a therapeutic antiarrhythmic effect was observed. Repeated applications at the maximum daily dose level did not increase blood drug concentration. Transdermal administration, in contrast to these patches, can result in systemic effects, but can be placed anywhere on the body, unlike these lidocaine patches, which need to be applied directly over the painful site.

Transmucosal analgesia

Buccal fentanyl (Actiq) is an alternative method of fentanyl administration, which acts more immediately than transdermal application. This formulation has an onset of pain relief within 5 to 10 minutes but is of short duration. It looks similar to the mouth-cleaning swabs that intensive care unit patients currently use for oral hygiene. When the matrix is dissolved, 25% of the dose is absorbed and 75% of the dose is swallowed, and of this only one-third is bioavailable.[33] Buccal fentanyl is indicated only for management of breakthrough pain in opiate-tolerant patients and is contraindicated in patients who have not been on opiate therapy. The term *opiate-tolerant* is reserved for patients who are on at least 60 mg morphine per day or an equivalent dose of other opiates.[34]

Butorphanol is a mixed agonist/antagonist opioid analgesic that is also available for transmucosal use in a nasal-systemic formulation. One spray through the nostril is the normal dose, with an onset of action within 15 minutes.

Combination therapy

There are different strategies in controlling postoperative pain in the chronic pain patient. Postoperatively, one of the most important issues is obtaining early control of pain. If one initially lets the pain get very severe

and out of hand, it is very difficult to subsequently gain control. Other important issues in getting control of pain include use of adjuvant analgesics and frequent pain assessment. "Combination analgesia" refers to use of two or more agents with different yet complementary mechanisms of action. The severity of dose-related side effects may be reduced in this manner because lower doses of each agent are used. An example of this is use of opioids together with NSAIDS. Opioids have multiple adverse reactions, including ileus. Multimodal analgesic therapy could lead to lower dose of opioids use, thereby reducing incidence of postoperative ileus.

Other therapies

There are other effective alternative therapies for treating pain. Such alternative therapies include biofeedback and guided imagery. Guided imagery involves images such as a speedometer at 100 miles per hour, which the patient is then asked, through relaxation techniques, to decrease to 70 miles per hour. Such guided imagery has been shown to be effective at decreasing both pre- and postoperative cortisol levels, decreasing postoperative pain, and decreasing analgesic use.[35] Guided imagery has also been shown in a prospective randomized trial in patients undergoing colon and rectal operations to decrease patient anxiety preoperatively, decrease pain postoperatively, and significantly decrease patient opioid requirements (ie, from 326 mg morphine postoperatively in patients not receiving guided imagery to 185 mg morphine in patients receiving guided imagery).[36]

TWO ILLUSTRATIVE CASES

To illustrate how difficult it can be to manage chronic pain patients, we describe two challenging patients we treated recently. The first is a 67-year-old woman with a longstanding partial small bowel obstruction, a 30-year history of Crohn's disease, and 15 earlier laparotomies. Her personal physicians had placated her reports of abdominal pain with large quantities of oxycodone. She underwent an operation at our institution with an extensive lysis of adhesions, repair of an existing enterocutaneous fistula, and insertion of a gastrostomy tube and a jejunostomy tube. Postoperatively, the patient experienced withdrawal pain each time her opioids were reduced, which was also associated with chronic nausea. This patient received methadone through her gastrostomy tube and had a transdermal fentanyl patch applied postoperatively. Until these became effective, she was placed on a Dilaudid PCA with a continuous IV dose, in addition to an on-demand dose. She was also given oxycodone with a sip of water for breakthrough pain, as needed.

The second chronic pain patient was a 52-year-old man with a giant rectal villous adenoma. The patient had a 20-year history of IV drug abuse and, as a consequence, had contracted hepatitis C. He was currently in a stable and successful methadone treatment program, but now had to undergo anterior resection for removal of this large upper rectal polyp. This patient was also placed on a Dilaudid PCA pump with both continuous IV and on-demand doses. His home methadone dose was resumed on postoperative day 2. An important issue in patients with chronic pain is whether or not one should keep them npo for oral medication after operation. If their pain is managed well by oral medication, why stop this after the operation? One should never upset a "steady state." In addition, use of nasogastric tubes should be avoided, if at all possible, because their use is associated with increased patient discomfort, increased air swallowing, and increased abdominal distention.

In conclusion, in caring for the chronic pain patient, it is especially important to realize that there is a significant risk of both overdosing and undertreating pain. These patients demand frequent assessment of their actual pain control. Pain management is frequently facilitated by using combination of analgesia and adjuvant analgesics. These new approaches to pain management will change the way we practice surgery and appear likely to improve patient care.

REFERENCES

1. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg 2003;97:534–540.
2. Hasenbring M, Hallner D, Klasen B. Psychological mechanisms in the transition from acute to chronic: over- or underrated? Schmerz 2001;15:442–447.
3. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. Clin J Pain 1996;12:50–55.
4. Robeznieks A. States get feds' help with Rx monitoring. Amednews.com [serial online]. 2004; Nov. 1. Available at: http://www.ama-assn.org/amednews/2004/11/01/prsa1101.htm. Accessed April 28, 2005.
5. Rapp SE, Ready LB, Nessly ML. Acute pain management in patients with prior opioid consumption: a case-controlled retrospective review. Pain 1995;61:195–201.
6. Eisenach JC, Grice SC, Dewan DM. Patient-controlled analge-

sia following cesarean section: a comparison with epidural and intramuscular narcotics. Anesthesiology 1988;68:444–448.
7. Harrison DM, Sinatra R, Morgese L, Chung JH. Epidural narcotic and patient-controlled analgesia for post-cesarean section pain relief. Anesthesiology 1988;68:454–457.
8. Miaskowski C, Crews J, Ready LB, et al. Anesthesia-based pain services improve the quality of postoperative pain management. Pain 1999;80:23–29.
9. Finlay RJ, Keeri-Szanto M, Boyd D. New analgesic agents and techniques shorten port-operative hospital stay. Pain 1984; 19:S397.
10. Cousins M. Acute and postoperative pain. In: Wall P, Melzack R, eds. Textbook of pain. New York: Churchill Livingstone; 1999:357–385.
11. Nimmo WS. Effect of anaesthesia on gastric motility and emptying. Br J Anaesth 1984;56:29–36.
12. Hutchinson TA, Flegel K, Kramer M, et al. Frequency, severity, and risk factors for adverse drug reactions in adult outpatients: a prospective study [abstract]. J Chronic Dis 1986;39:533.
13. Shorr R, Griffin M, Daugherty J, et al. Opioid analgesics and risk of hip fracture in the elderly. J Gerontol 1992;47:M111.
14. Kain ZN, Sevarino F, Pincus S, et al. Attenuation of the preoperative stress response with midazolam: effects on postoperative outcomes. Anesthesiology 2000;93:141–147.
15. Connelly NR, Reuben SS, Albert M, Page D. Use of preincisional ketorolac in hernia patients: intravenous versus surgical site. Reg Anesth 1997;22:229–232.
16. Altunkaya H, Ozer Y, Kargi E, et al. The postoperative analgesic effect of Tramadol when used as subcutaneous local anesthetic. Anesth Analg 2004;99:1461–1464.
17. Morrison JE Jr, Jacobs VR. Reduction or elimination of postoperative pain medication after mastectomy through use of a temporarily placed local anesthetic pump vs control group. Zentralbl Gynakol 2003;125:17–22.
18. Carli F, Mayo N, Klubien K, et al. Epidural analgesia enhances functional exercise capacity and health-related quality of life after colonic surgery: results of a randomized trial. Anesthesiology 2002;97:540–549.
19. Cullen DJ, Bogdanov E, Htut N. Spinal epidural hematoma occurrence in the absence of known risk factors: a case series. J Clin Anesth 2004;16:376–381.
20. Viscusi ER, Martin G, Hartrick CT, et al. Forty-eight hours of postoperative pain relief after total hip arthroplasty with a novel, extended-release epidural morphine formulation. Anesthesiology 2005;102:1014–1022.
21. Wood M. Opioid agonists and antagonists. In: Wood M, Wood A, eds. Drugs and anesthesia, pharmacology for anesthesiologists. Baltimore: Williams & Wilkins 1990:129–178.
22. Physicians' desk reference. 58th ed. Montvale, NJ: Thomson PDR; 2004:2495−2496.
23. Dubois RN, Abramson SB, Crofford L, et al. Cyclo-oxygenase in biology and disease. FASEB J 1998;12:1063–1073.
24. Keane WF. Physicians' notification letter: Merck announces voluntary worldwide withdrawal of VIOXX. Available at: http://www.vioxx.com/rofecoxib/vioxx/hcp/hcp_notification_physicians.jsp. Accessed April 28, 2005.
25. USFDA. Alert for healthcare professionals Valdecoxib (marketed as Bextra). Food and Drug Administration Web site. Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/valdecoxibHCP.htm. Accessed April 28, 2005.
26. Feinberg SD. Prescribing analgesics. How to improve function and avoid toxicity when treating chronic pain? Geriatrics 2000; 44:49–50.
27. Bryson HM, Wilde MI. Amiptriptyline. A review of its pharmacological properties and therapeutic use in chronic pain states. Drugs Aging 1996;8:459–476.
28. Muijsers RB, Wagstaff AJ. Transdermal fentanyl: an updated review of its pharmacological properties and therapeutic efficacy in chronic cancer pain control. Drugs 2001;61:2289–2307.
29. Chelly JE, Grass J, Houseman TW, et al. The safety and efficacy of a fentanyl patient-controlled transdermal system for acute postoperative analgesia: a multicenter, placebo-controlled trial. Anesth Analg 2004;98:427–433.
30. Lehmann LJ, DeSio JM, Radvany T, Bikhazi GB. Transdermal fentanyl in postoperative pain. Reg Anesth 1997;22:24–28.
31. Physicians' desk reference. 58th ed. Montvale, NJ: Thomson PDR; 2004:1238−1239.
32. Comer AM, Lamb HM. Lidocaine patch 5%. Drugs 2000;59: 245–249.
33. Rees E. The role of oral transmucosal fentanyl citrate in the management of breakthrough cancer pain. Int J Palliat Nurs 2002;8:304–308.
34. Physicians' desk reference. 58th ed. Montvale, NJ: Thomson PDR; 2004:1151−1155.
35. Manyande A, Berg S, Gettins D, et al. Preoperative rehearsal of active coping imagery influences subjective and hormonal responses to abdominal surgery. Psychosom Med 1995;57:177–182.
36. Tusek DL, Church JM, Strong SA, et al. Guided imagery: a significant advance in the care of patients undergoing elective colorectal surgery. Dis Colon Rectum 1997;40:172–178.